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Case 7280&

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Matter of:

Continuation under 35 USC § 120
of United States Application of :
CHANCHAL GHOSH, et al. :
U.S. Appln. No. 09/529,905
Int'l Appln No. PCT/US98/22588 :
Int'l Filing Date of 23 October 1998 :
Entitled: CLEANING
COMPOSITIONS
CONTAINING MULTIPLY-
SUBSTITUTED
PROTEASE VARIANTS

PRELIMINARY AMENDMENT

Commissioner for Patents
Box PATENT APPLICATION
Washington, D.C. 20231
Dear Sir:

Prior to Examination and computation of the fees for entering the above-captioned Continuation Application into the United States, please preliminarily amend the above-identified application as follows and consider the following Remarks.

AMENDMENTS

In the Specification

Please insert the following text before "Field of the Invention,"

Cross-Reference to Related Applications

This application is a continuation under 35 USC §120 of Application Serial No. 09/529,905, which is a 371 of PCT/US98/22588 filed on 23 October 1998, which claims priority under 35 USC 120 to US Application No. 08/956,323, filed on 23 October 1997, US Application No. 08/956,564, filed on 23 October 1997, and US Application No. 08/956,324, filed on 23 October 1997.

In the Claims

Please cancel Claims 1-46 and insert therefor new Claims 47-71 as follows.

47 (New). A fabric and/or dishwashing and/or hard surface cleaning composition comprising:

(a) an effective amount of a protease variant wherein said protease variant includes a substitution of an amino acid residue with another naturally occurring amino acid residue at an amino acid residue position corresponding to position 103 of *Bacillus amyloliquefaciens* subtilisin in combination with a substitution of an amino acid residue with another naturally occurring amino acid residue at one or more amino acid residue positions corresponding to positions 1, 3, 4, 8, 9, 10, 12, 13, 16, 17, 18, 19, 20, 21, 22, 24, 27, 33, 37, 38, 42, 43, 48, 55, 57, 58, 61, 62, 68, 72, 75, 76, 77, 78, 79, 86, 87, 89, 97, 98, 99, 101, 102, 104, 106, 107, 109, 111, 114, 116, 117, 119, 121, 123, 126, 128, 130, 131, 133, 134, 137, 140, 141, 142, 146, 147, 158, 159, 160, 166, 167, 170, 173, 174, 177, 181, 182, 183, 184, 185, 188, 192, 194, 198, 203, 204, 205, 206, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 222, 224, 227, 228, 230, 232, 236, 237, 238, 240, 242, 243, 244, 245, 246, 247, 248, 249, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 265, 268, 269, 270, 271, 272, 274 and 275 of *Bacillus amyloliquefaciens* subtilisin; wherein when said protease variant includes a substitution of amino acid residues at positions corresponding to positions 103 and 76, there is also a substitution of an amino acid residue at one or more amino acid residue positions other than amino acid residue positions corresponding to positions 27, 99, 101, 104, 107, 109, 123, 126, 128, 166, 204, 206, 210, 216, 217, 218, 222, 260, 265 or 274 of *Bacillus amyloliquefaciens* subtilisin; and

(b) one or more cleaning adjunct materials.

48. (New) The cleaning composition according to Claim 47 wherein said protease variant is derived from a *Bacillus* subtilisin.

49. (New) The cleaning composition according to Claim 47 wherein said protease variant includes substitutions of the amino acid residues at position 103 and at one or more of the following positions: 236 and 245.

50. (New) The cleaning composition according to Claim 47 wherein said protease variant includes a substitution set selected from the group consisting of:

12/102/103/104/159/212/232/236/245/248/252;

12/76/103/104/130/170/185/222/243/245;

12/76/103/104/130/222/245/261; 12/76/103/104/222/245;

12/76/103/104/130/222/245;

61/68/103/104/159/232/236/245/248/252; 62/103/104/159/213/232/236/245/248/252;

62/103/104/109/159/213/232/236/245/248/252; 62/103/104/159/232/236/245/248/252;

62/101/103/104/159/212/213/232/236/245/248/252;

62/103/104/130/159/213/232/236/245/248/252;

68/103/104/159/232/236/245/248/252/270;

68/103/104/159/185/232/236/245/248/252; 68/103/104/159/210/232/236/245/248/252;

68/103/104/159/185/210/232/236/245/248/252;

68/103/104/159/213/232/236/245/248/252;

68/103/104/159/230/232/236/245;

68/76/103/104/159/209/232/236/245;

68/103/104/232/236/245/248/257/275;

68/103/104/213/232/236/245/248/252;

68/103/104/159/232/236/245/248/252;

68/103/104/159/209/232/236/245;

68/76/103/104/159/236;

68/76/103/104/159/236/245;

68/76/103/104/159/232/236/245;

68/103/104/159/232/236/245/252;

68/103/104/159/232/236/245;

68/103/104/159/232/236/245/257;

68/76/103/104/159/211/232/236/245;

68/76/103/104/159/215/232/236/245;

68/103/104/159/210/232/236/245;

68/103/104/159/213/232/236/245/260;

68/76/103/104/159/213/232/236/245/260;

68/103/104/159/236;

68/76/103/104/159/210/232/236/245/260;

68/103/104/159/236/245;

68/103/104/159/183/232/236/245/248/252;

68/76/103/104/159/236/245;

68/103/104/232/236/245/257/275;

68/103/104/159/213/232/236/245;

76/103/222/245;

76/103/104/159/232/236/245;

76/103/104/159/213/232/236/245/260;

76/103/104/159;

76/103/104/131/159/232/236/245/248/252; 76/103/104/222/245;

97/103/104/159/232/236/245/248/252;

98/102/103/104/159/212/232/236/245/248/252; 98/103/104/159/232/236/245/248/252;

101/103/104/159/232/236/245/248/252; 102/103/104/159/232/236/245/248/252;
103/104/159/232/236/245; 103/104/159/232/236/245/248/252;
103/104/159/205/209/232/236/245/257 103/104/159/232/245/248/252;
103/104/159/205/209/210/232/236/245/257; 103/104/159/213/232/236/245/248/252;
103/104/159/217/232/236/245/248/252; 103/104/130/159/232/236/245/248/252;
103/104/159/230/236/245; 103/104/159/236/245;
103/104/159/248/252/270; 103/104/131/159/232/236/245/248/252;
103/104/159/205/209/232/236/245; and 103/104/159/232/236/245/257.

51. (New) The cleaning composition according to Claim 50 wherein said protease variant includes a substitution set selected from the group consisting of:

12R/76D/103A/104T/130T/222S/245R;
12R/76D/103A/104I/222S/245R;
12R/102A/103A/104I/159D/212G/232V/236H/245R/248D/252K;
12R/76D/103A/104T/130G/222S/245R/261D;
12R/76D/103A/104T/130G/170S/185D/222S/243D/245R;
61E/68A/103A/104I/159D/232V/236H/245R/248D/252K;
62D/103A/104I/109R/159D/213R/232V/236H/245R/248D/252K;
62D/103A/104I/159D/213R/232V/236H/245R/248D/252K;
62D/103A/104I/159D/232V/236H/245R/248D/252K;
62D/103A/104I/159D/232V/236H/245R/248D/252K;
62D/103A/104I/130G/159D/213R/232V/236H/245R/248D/252K;
62D/101G/103A/104I/159D/212G/213R/232V/236H/245R/248D/252K;
68A/76D/103A/104I/159D/213R/232V/236H/245R/260A;
68A/103A/104I/159D/236H;
68A/103A/104I/159D/236H/245R;
68A/76D/103A/104I/159D/210I/232V/236H/245R/260A;
68A/103A/104I/159D/183D/232V/236H/245R/248D/252K;
68A/103A/104I/159D/209W/232V/236H/245R;
68A/76D/103A/104I/159D/211R/232V/236H/245R;
68A/76D/103A/104I/159D/215R/232V/236H/245R;
68A/103A/104I/159D/213R/232V/236H/245R/260A;
68A/76D/103A/104I/159D/236H;
68A/76D/103A/104I/159D/236H/245R;
68A/76D/103A/104I/159D/232V/236H/245R;
68A/103A/104I/159D/232V/236H/245R/252K;
68A/103A/104I/159D/232V/236H/245R;
68A/103A/104I/159D/232V/236H/245R/257V;

68A/103A/104I/159D/185D/232V/236H/245R/248D/252K;
68A/103A/104I/159D/210L/232V/236H/245R/248D/252K;
68A/103A/104I/159D/185D/210L/232V/236H/245R/248D/252K;
68A/103A/104I/159D/213E/232V/236H/245R/248D/252K;
68A/103A/104I/159D/230V/232V/236H/245R;
68A/76D/103A/104I/159D/209W/232V/236H/245R;
68A/103A/104I/232V/236H/245R/248D/257V/275H;
68A/103A/104I/232V/236H/245R/257V/275H;
68A/103A/104I/213E/232V/236H/245R/248D/252K;
68A/103A/104I/159D/232V/236H/245R/248D/252K;
68A/103A/104I/159D/210I/232V/236H/245R;
68A/103A/104I/159D/210L/232V/236H/245R;
68A/103A/104I/159D/213G/232V/236H/245R;
68A/103A/104I/159D/232V/236H/245R/248D/252K/270A;
76D/103A/222S/245R;
76D/103A/104I/159D/232V/236H/245R;
76D/103A/104I/159D;
76D/103A/104I/222S/245R;
76D/103A/104I/131V/159D/232V/236H/245R/248D/252K;
76D/103A/104I/159D/213R/232V/236H/245R/260A;
97E/103A/104I/159D/232V/236H/245R/248D/252K;
98L/103A/104I/159D/232V/236H/245R/248D/252K;
98L/102A/103A/104I/159D/212G/232V/236H/245R/248D/252K;
101G/103A/104I/159D/232V/236H/245R/248D/252K;
102A/103A/104I/159D/232V/236H/245R/248D/252K;
103A/104I/159D/232V/236H/245R/248D/252K;
103A/104I/159D/213R/232V/236H/245R/248D/252K;
103A/104I/130G/159D/232V/236H/245R/248D/252K;
103A/104I/159D/230V/236H/245R;
103A/104I/159D/217E/232V/236H/245R/248D/252K;
103A/104I/159D/236H/245R;
103A/104I/159D/248D/252K/270V;
103A/104I/159D/232V/236H/245R;
103A/104I/159D/205I/209W/232V/236H/245R;
103A/104I/159D/232V/236H/245R/257V;
103A/104I/159D/205I/209W/232V/236H/245R/257V;
103A/104I/131V/159D/232V/236H/245R/248D/252K;
103A/104I/159D/205I/209W/210I/232V/236H/245R/257V; and

52. (New) The cleaning composition according to Claim 47 wherein said cleaning adjunct materials are selected from the group consisting of surfactants, solvents, buffers, enzymes, soil release agents, clay soil removal agents, dispersing agents, brighteners, suds suppressors, fabric softeners, suds boosters, enzyme stabilizers, builders, other bleaching agents, dyes, perfumes, chelants and mixtures thereof.

53. (New) The cleaning composition according to Claim 52 wherein said cleaning adjunct materials comprise at least one deterotive surfactant.

54. (New) The cleaning composition according to Claim 53 wherein the cleaning adjunct materials comprise at least about 0.1% surfactant by weight of the composition, said surfactant comprising materials selected from the group consisting of alkyl benzene sulfonates, primary alkyl sulfates, secondary alkyl sulfates, alkyl alkoxy sulfates, alkyl alkoxy carboxylates, alkyl polyglycosides and their corresponding sulfated polyglycosides, alpha-sulfonated fatty acid esters, alkyl and alkyl phenol alkoxylates, betaines and sulfobetaines, amine oxides, N-methyl glucamides, nonionic primary alcohol ethoxylates, nonionic primary alcohol mixed ethoxy/propoxy, and mixtures thereof.

55. (New) The cleaning composition according to Claim 54 further comprising at least about 5% builder selected from the group consisting of zeolites, polycarboxylates, layered silicates, phosphates, and mixtures thereof.

56. (New) The cleaning composition according to Claim 52 wherein said cleaning adjunct materials comprise at least one deterotive enzyme selected from the group consisting of cellulases, lipases, amylases, phospholipases, other proteases, peroxidases and mixtures thereof.

57. (New) The cleaning composition according to Claim 52 wherein said cleaning adjunct materials comprise at least one bleaching agent selected from the group consisting of percarbonates, perborates and mixtures thereof, and optionally further comprising at least one bleach activator selected from the group consisting of benzyloxybenzenesulphonate (BOBS), nonanoyloxybenzenesulphonate (NOBS), decanoxybenzenesulphonate (C₁₀-OBS), octanoyloxybenzenesulphonate (C₈-OBS), perhydrolyzable esters, 4-[N-(nonaoyl) amino hexanoyloxy]-benzene sulfonate sodium salt (NACA-OBS), lauryloxybenzenesulphonate (LOBS or C₁₂-OBS), 10-undecenoyloxybenzenesulfonate

(UDOBS or C₁₁-OBS with unsaturation in the 10 position), and decanoxyloxybenzoic acid (DOBA) and mixtures thereof, and further optionally comprising at least one bleach catalyst.

58. (New) The cleaning composition according to Claim 47 wherein said cleaning composition is a fabric cleaning composition, in the form of a liquid, granule, bar, tablet, gel, powder or foam, comprising at least about 5% surfactant and at least about 5% builder by weight of the composition.

59. (New) The cleaning composition according to Claim 47 wherein said cleaning composition is a fabric cleaning composition comprising:

- (a) from about 0.0001% to about 10% by weight of said protease variant;
- (b) at least about 5% by weight of a surfactant selected from the group consisting of alkyl benzene sulfonates, primary alkyl sulfates, secondary alkyl sulfates, alkyl alkoxy sulfates, alkyl alkoxy carboxylates, alkyl polyglycosides and their corresponding sulfated polyglycosides, alpha-sulfonated farry acid esters, alkyl and alkyl phenol alkoxylates, betaines and sulfobetaines, amine oxides, N-methyl glucamides, nonionic primary alcohol ethoxylates, nonionic primary alcohol mixed ethoxy/propoxy, and mixtures thereof; and wherein further the builder is selected from the group consisting of zeolites, polycarboxylates, layered silicates, phosphates, and mixtures thereof; and
- (c) at least about 5% by weight of a builder selected from the group consisting of zeolites, polycarboxylates, layered silicates, phosphates, and mixtures thereof.

60. (New) The cleaning composition according to Claim 59 is in the form of a concentrated granular fabric cleaning composition comprising at least about 15% surfactant.

61. (New) A method for cleaning fabric, said method comprising contacting a fabric in need of cleaning with a cleaning composition according to Claim 58.

62. (New) A method for cleaning fabric, said method comprising contacting a fabric in need of cleaning with a cleaning composition according to Claim 59.

63. (New) The cleaning composition according to Claim 47 wherein said cleaning composition is a dishwashing composition, in the form of a liquid, granule, powder, gel or tablet, comprising:

- (a) from about 0.0001% to about 10% by weight of said protease variant; and
- (b) from about 0.1% to about 10% by weight of a surfactant.

64. (New) A method for cleaning dishes, said method comprising contacting a dish in need of cleaning with a cleaning composition according to Claim 63.

65. (New) A personal cleansing composition comprising:

(a) an effective amount of a protease variant wherein said protease variant includes a substitution of an amino acid residue with another naturally occurring amino acid residue at an amino acid residue position corresponding to position 103 of *Bacillus amyloliquefaciens* subtilisin in combination with a substitution of an amino acid residue with another naturally occurring amino acid residue at one or more amino acid residue positions corresponding to positions 1, 3, 4, 8, 9, 10, 12, 13, 16, 17, 18, 19, 20, 21, 22, 24, 27, 33, 37, 38, 42, 43, 48, 55, 57, 58, 61, 62, 68, 72, 75, 76, 77, 78, 79, 86, 87, 89, 97, 98, 99, 101, 102, 104, 106, 107, 109, 111, 114, 116, 117, 119, 121, 123, 126, 128, 130, 131, 133, 134, 137, 140, 141, 142, 146, 147, 158, 159, 160, 166, 167, 170, 173, 174, 177, 181, 182, 183, 184, 185, 188, 192, 194, 198, 203, 204, 205, 206, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 222, 224, 227, 228, 230, 232, 236, 237, 238, 240, 242, 243, 244, 245, 246, 247, 248, 249, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 265, 268, 269, 270, 271, 272, 274 and 275 of *Bacillus amyloliquefaciens* subtilisin; wherein when said protease variant includes a substitution of amino acid residues at positions corresponding to positions 103 and 76, there is also a substitution of an amino acid residue at one or more amino acid residue positions other than amino acid residue positions corresponding to positions 27, 99, 101, 104, 107, 109, 123, 126, 128, 166, 204, 206, 210, 216, 217, 218, 222, 260, 265 or 274 of *Bacillus amyloliquefaciens* subtilisin; and

(b) one or more cleaning adjunct materials.

66 (New). The personal cleansing composition according to Claim 65 wherein said personal cleansing composition comprises:

(a) from about 0.001% to about 5% by weight of said protease variant;
(b) from about 0.1% to about 95% by weight of a surfactant system comprising a surfactant selected from the group consisting of anionic carboxylates, amine oxides, alkyl glucosides, glucose amides, alkyl sulfates, alkyl ether sulfates, acyl isethionates, alkyl sulfosuccinates, alkyl phosphate esters, ethoxylated phosphate esters, alkyl glyceryl ether sulfonates and mixtures thereof; and
(c) optionally, from about 0.05% to about 50% by weight of an enzyme stabilizer.

67. (New) The personal cleansing composition according to Claim 66 wherein said surfactant is soap at a level of at least about 2% by weight of the cleaning composition.

68. (New) The personal cleansing composition according to Claim 67 wherein the ratio of soap to protease variant is from about 2,000:1 to about 8:1.

69. (New) A method for personal cleansing, said method comprising contacting a part of the human or lower animal body in need of cleaning with a cleaning composition according to Claim 65.

70. (New) A method for pretreating a fabric in need of cleaning, said method comprising contacting said fabric prior to washing said fabric with an aqueous solution containing a surfactant with a cleaning composition according to Claim 58 .

71. (New) A method for pretreating a fabric in need of cleaning, said method comprising contacting said fabric prior to washing said fabric with an aqueous solution containing a surfactant with a cleaning composition according to Claim 59.

REMARKS

Claims 1-46 have been canceled without prejudice. Claims 47-71 have been renumbered and amended to particularly point out and distinctly claim the subject matter of the present invention. Antecedent basis for Claims 47-71 is found throughout the specification and original claims.

CONCLUSION

Applicants have made an earnest effort to place the present claims in condition for allowance. WHEREFORE, entry of the amendments provided herewith, and allowance of Claims 47-71, as amended, are respectfully requested.

Respectfully submitted,

CHANCHAL GHOSH, et al.

By



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